PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PN0283-PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/NO 03/00352	International filing date *(day/month/year)* 24.10.2003	Priority date *(day/month/year)* 25.10.2002
International Patent Classification (IPC) or both national classification and IPC A61K51/00		
Applicant AMERSHAM HEALTH AS et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.05.2004	06.09.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Beeck, M Telephone No. +49 89 2399-8473

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/NO 03/00352

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-10 received on 15.07.2004 with letter of 15.07.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-10
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

D1: HARALD E. MÖLLER ET AL: "MRI of the Lungs Using Hyperpolarized Noble Gases" MAGNETIC RESONANCE IN MEDICINE, vol. 47, 2002, pages 1029-1051, XP002272037

D2: WO 01/55656 A (OXFORD INSTR SUPERCONDUCTIVITY ;KALECHOFSKY NEAL FREDERICK (US)) 2 August 2001 (2001-08-02)

D3: WO 00/23797 A (UNIV SYRACUSE) 27 April 2000 (2000-04-27)

SECTION V:

Closest prior art document is D3 from which the subject-matter of the present application differs in that the DNP method is selected from several methods of hyperpolarization and a solvent or a mixture of solvents is used, which leads to a higher polarization.

Since this was not obvious for the person skilled in the art, the subject-matter of the claims involves an inventive step.

Claims:

1. A method for producing hyperpolarized ^{129}Xe comprising
   a) preparing a mixture of xenon, an additive and a free radical
   b) hyperpolarizing said mixture according to the DNP method to obtain hyperpolarized ^{129}Xe and
   c) optionally separating said xenon from the other components of the mixture.

2. A method according to claim 1 wherein the additive is at least one solvent or a mixture of solvents which has good glass-forming properties and/or lipophilic properties.

3. A method according to claim 1 and 2, wherein the additive is a solvent or a mixture of solvents selected from the group consisting of straight chain or branched C_6-C_{12}-alkanes, C_5-C_{12}-cycloalkanes, fatty alcohols, fatty esters, substituted benzene derivatives, mono- or polyfluorinated solvents, single chained alcohols and glycols.

4. A method according to claims 1 to 3 wherein the mixture in step a) is prepared from liquid xenon.

5. A method according to claims 1 to 4 wherein the mixture in step a) is prepared by condensing xenon gas on the top of the additive and the free radical, warming the components until xenon and the additive are in a liquid state and mixing the components until a homogeneous mixture is obtained.

6. A method according to claims 1 to 5 wherein in step b) ^{129}Xe is directly hyperpolarized.

7. A method according to claims 1 to 6 wherein in step b) the NMR active nuclei of the additive are hyperpolarized and this polarization is subsequently transferred to ^{129}Xe by a cross-polarization sequence.

8. A method according to claims 1 to 7 wherein xenon enriched with ^{129}Xe is used.

9. A method according to claims 1 to 8 wherein in step c) xenon is separated from the other components of the mixture by warming the mixture until xenon is in the gas state and collecting said xenon in a suitable container.

10. A method for the production of a contrast agent comprising

a) preparing a mixture of xenon, an additive and a free radical

b) hyperpolarizing said mixture according to the DNP method to obtain hyperpolarized ^{129}Xe

c) separating said xenon from the other components of the mixture, and

d) optionally condensing the separated xenon again.

12. Use of DNP - hyperpolarized ^{129}Xe for the manufacture of a contrast agent for the use in magnetic resonance imaging of the human or non-human animal body, preferably of the lungs of the human or non-human animal body.